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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/399,120	09/20/1999	DESMOND MASCARENHAS	220952029300	1886

7590 08/22/2006

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EXAMINER	
GUPTA, ANISH	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 08/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/399,120	MASCARENHAS, DESMOND	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,16 and 18-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-10,16,18-21,23-44 and 47-50* is/are allowed.

6)☒ Claim(s) *22,45 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *7-26-06*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Board of Appeals rendered a decision on this Application on the issue of 112 First Paragraph of enablement. The Board reversed the outstanding rejection and hence, the rejection under 112 First Paragraph has been withdrawn. However, in reviewing the Application, support for the claimed limitation of claims 22, 45 and 46 could not be ascertained. Thus, a new ground for rejection under 112 First Paragraph, New Matter follows below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22, 45, 46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of slowing or treating cancer using an effective amount of null insulin-like growth factor I (null-IGF-I). The claims in question recite specific null-IGF-I that have alterations of residues 28-37 replaced with four glycine residues (claim 22), and specifically mutated IGF molecules as recited in claims 45-46.

Lack of *Ipsis Verbis* Support

The specification is void of any literal support for the specific IGF molecules claimed. The specification, on page 10, provides support for the null IGF molecule Y60L, where the 60th residue of the IGF molecule has been replaced by Leucine. However, the specification does not provide any literal support for other Null IGF-1 molecules claimed such as [Ala-31, Leu-60 IGF-I], [Leu24, Leu 60, IGF-1], [Leu24, Ala31, Leu60] IGF-I, [1-27, Gly4, 38-70]; [Ser24]IGF-1, and [Leu24, 1-62]IGF-1, and any IGF molecule where residues 28-37 have been replaced with four glycine residues.

Lack of Implicit or Inherent Support

"While there is no in *haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure." See MPEP 2163. Thus, support can be furnished implicitly or inherently for a specifically claimed limitation. However the specification lack any implicit or inherent support for the claimed IGF molecules. On page 5, which defines Null IGF, the specification states that Null-IGF include "variants in which one or more which one or more of IGF-I's tyrosine residues (i.e., residues 24, 31, or 60) are replaced with non-aromatic residues (i.e, other than tyrosine, phenylalsnine or tryptophan), variants where amino acid residues 49, 50, 51, 53, 55 and 56 are altered (for example, where residues 49-50 are altered to Thr-ser- Ile or where residues 55-56 are altered to Tyr-G1n), and combinations thereof." The specification fails to provide any support that "non-aromatic" amino acids specifically include Serine, providing support for [Ser24]IGF-1. In the context of non aromatic amino acids, the specification only provides support for the substitution of leucine in position 60.

Further, the definitions do not lead one to conclude that truncated analogs such as [Leu24, 1-62]IGF-1 and analogs with four glycine residues are within the meaning of the Null IGF definition.

In a telephone interview, Applicants stated that support for the specific analogs could be found in the reference of Cascieri et al. (1988 and 1989), Bayne et al. (1990), and Baxter et al. (1992), cited on page 5 of the specification and which are incorporated by reference into the disclosure. However, this does not provide support for the specific IGF-1 molecules for two reasons.

First, 37 CFR 1.57(c) prohibits incorporation by reference to essential subject matter using non-patent literature. 37 CFR 1.57(c) recites:

> (c) " **Essential material** " may be incorporated by reference, but **only by way of an incorporation by reference to a U.S. patent or U.S. patent application publication,** which patent or patent application publication does not itself incorporate such essential material by reference. "Essential material " is material that is necessary to:
> (1) Provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112;
> (2) Describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112; or
> (3) Describe the structure, material, or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 U.S.C. 112."

The claimed subject matter is "Essential material" since it provide it provides written description as defined in sub paragraph (1). Since the "Essential material," claimed in the instant application, is not recited in a "U.S. patent or U.S. patent application publication, which patent or patent application publication does not itself incorporate such essential material by reference," it is improper to provide support via the "incorporation by reference" means.

Secondly the decision of Ex Parte Raible, 8 USPQ2d 1709 (BPAI) is controlling in this case. In Raible, Appellants attempted to use the doctrine of incorporation by reference to provide support for a claimed limitation. The Board stated the doctrine of incorporation by reference could not be

used by Appellant since the specification did not contain a specific indication of the features disclosed by the incorporating reference which corresponded to the features specifically claimed. See Raible at 1710. Further the specification did not "identify the specific portions of the patent which appellant may have intended to rely upon to supplement his disclosure." Raible at 1710. The Board concluded "[t]he purpose of incorporation by reference in an application of matter elsewhere written down is for economy, amplification, or clarity of exposition, by means of an *incorporating statement clearly identifying the subject matter which is incorporated and where it is to be found."* Raible at 1710.

Here, the instant specification fails to provide "an incorporating statement clearly identify the subject which is corporate and where it is to be found." Bayne reference recites teaches seven IGF analogs that have point mutation at positions 24, 31, 60, multiple mutations at 24, 31, and 60 that meet the definition of Null IGF, Cascieri et al. (1989) disclose one IGF molecules that falls within the claimed definition, Baxter (1992) discloses numerous analogs, such as [Tyr 15, Leu16] IGF-I, [Gln3, Ala4, Tyr15, Leu16] IGF-1, [Ser24 IGF I], [1-62 IGF 1], [Leu 24, 1-62] IG-1, [Tyr 55, Gln 56] IGF-1, [1-27, Gly4, 38-70] IGF-1, [1-27, Gly4, 38-62] IGF-1, thaat fall within Applicants definition of IGF, and Cascieri (1988) teahes three IGF molecules . Of these, only few have been claimed in the instant application. The instant specification does not provide any "statement clearly identify" that the specifically claimed IGF analogs fall within the definition of the claimed invention and are incorporated by reference. Hence, it cannot be said that the reference cited provide implicit or inherent support.

Allowable Subject Matter

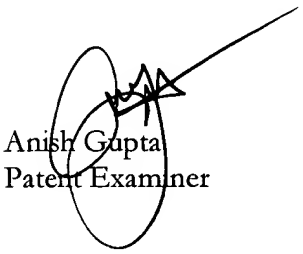
3. Claims 1-10, 16, 18-21, 23-44, 47-50 are drawn to a method of slowing the growth rate of a tumor or slowing progression of cancer, comprising: administering an effective amount of uncomplexed null insulin like growth factor I to subject having cancer (see claims 1 and 16).

The prior art of Jameson et al. (US5473054) teach IGF-1 analogs that are effective inhibiting cell proliferation, close to 100%. The IGF analog is effective against cells including: fibroblasts, smooth muscle cells, chondrocytes and osteoblasts, hemopoietic cells of various lineages and keratinocytes. The reference states that for instance, when using the IGF-1 analog, inhibition of the growth of fibroblasts, and fibroblast-like cells, of T-lymphocytes and of epithelial cells derived from carcinoma of the prostate was observed (see col. 6, lines 15-27). The reference further states that IGF analogs have the ability to inhibit the binding of natural IGF-1 to its cognate receptor, thereby inhibiting the action of the IGF-1 receptor (see col. 3, lines 7-12 and col. 8, lines 6-15).

This reference does not anticipate nor render obvious the claimed invention. The Board of Appeals, stated in their decision, "as taught by the specification, a null IGF-I has amino acid sequence alterations at one or more sites in the molecule, while retaining its ability to bind to IGFBP-3, but is altered in its receptor biding and/or activating properties" (see page 6 of the BPAI decision). This definition is recited on page 5 of the specification that states "As used herein, the term 'null IGF-I' refers to IGF-I which has amino acid sequence alterations at one or more sites in the molecule. Null IGF-I retains its ability to bind IGFBP-3, but is altered in its receptor binding and/or activating properties (e.g., <u>having little or no binding to the type 1 IGF receptor while maintaining its binding activities for the type 2 IGF receptor and the insulin receptor</u>)." Thus, null IGF has little or no binding to the type 1 IGF receptor. Since the analogs of Jameson et al. are competitive binders to the IGF-1 receptor 1, the IGF analogs of the prior art do not fall within the

definition of the claimed null IGF. Thus, the claimed invention is both novel and unobvious over the prior art of record.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (571) 272-0562. The fax phone number of this group is (571)-273-8300.



Anish Gupta
Patent Examiner